

REMARKS

A. Status of the Claims

Claims 1-3 were pending at the issuance of the instant Office Action. Claims 1-3 are rejected in the instant Office Action. No claims are amended, added, or canceled herein. Applicants thank the Examiner for the previous consideration of our submissions.

B. Rejections under 35 U.S.C. § 103(a)

The Action rejects all claims under 35 U.S.C. 103(a) as being obvious over Malfroy-Camine *et al.* (6,064,188) in view of Winkler *et al.* (Molecular Vision 1999).

The present invention is directed to the use of certain superoxide dismutase mimics to treat persons suffering from AMD, diabetic retinopathy, or retinal edema. MPEP §2143.03 requires that all claim limitations be considered in an obviousness determination, and the Board of Patent Appeal and Interferences (BPAI) recently confirmed that “obviousness requires a suggestion of all limitations in a claim.” *See In re Wada and Murphy*, Appeal 2007-3733, *citing CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Circ. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Applicants submit that none of the cited art teaches or suggests the use of the compounds in the instant claims to treat AMD, diabetic retinopathy, or retinal edema. In particular, it is submitted that Winkler *et al.* fail to cure the conceded deficiency in Malfroy-Camine *et al.*, and that the asserted combination of Malfroy-Camine *et al.* and Winkler *et al.* therefore fails to render the instant claims obvious.

The Action concedes that Malfroy-Camine *et al.* do not teach or suggest the use of the compounds in the instant claims for the treatment of AMD, diabetic retinopathy, or retinal edema (see page 3 of the Office Action mailed 12/28/07). Nevertheless, the Action rejects the instant claims, asserting that Winkler *et al.* provide the necessary disclosure. In particular, the Action contends that Winkler *et al.* teach a correlation between oxidation and macular degeneration and in particular the use of superoxide dismutase in preventing oxidative damage caused by macular degeneration (see page 3 of the Office Action mailed 12/28/07). Applicants respectfully traverse this contention.

The Action's obviousness rejection appears to be based primarily on the misguided reasoning that Winkler *et al.* teach a general concept that superoxide dismutase compounds can be used to treat macular degeneration. Applicants submit that the teaching of Winkler *et al.* is inadequate to support the Action's reasoning. As discussed below, Winkler *et al.* do not teach or suggest that any superoxide dismutase compound can be used to treat macular degeneration, diabetic retinopathy, or retinal edema.

The Action asserts that Winkler *et al.* teach the role of oxidation in relation to macular degeneration and the effect of superoxide dismutase in preventing oxidative damage caused by macular degeneration (see page 2 of the Office Action mailed 6/14/07). Applicants submit that the Action has mischaracterized the teaching of Winkler *et al.*, and erroneously relies upon the reference in arriving at the instant invention.

The Winkler reference is a review article that discusses "the *potential* role of oxidation in relation to age-related macular degeneration" (see Abstract of Winkler, emphasis added). However, Winkler *et al.* do not provide any data to support the proposition that superoxide dismutase specifically could be used to treat AMD. In addition, Winkler *et al.* confessed that "it remains unclear whether oxidation is a causative factor in the progression of AMD" (see second column, second page of Winkler *et al.*). Furthermore, Winkler *et al.* focus the majority of their discussion on studies involving non-enzyme antioxidants including glutathione (GSH), vitamin C, vitamin E, and carotenoids. Superoxide dismutase is merely mentioned as only one of many oxidants. Indeed, the teaching of Winkler *et al.* is not focused on superoxide dismutase, and fails to elaborate on the possible role of superoxide dismutase in the discussion of oxidants that may (or may not) be involved in AMD progression. Consequently, Applicants submit that Winkler *et al.* does not provide any motivation for one of skill in the art to consider using a superoxide dismutase compound to treat AMD.

Furthermore, as stated in MPEP 2143.02(II), "obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness" (citing *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976)). Applicants have provided evidence that there was no reasonable expectation of success for using superoxide dismutase compounds to treat AMD, diabetic retinopathy, and/or retinal edema based on the teaching of

Winkler *et al.* or based on the knowledge of one skilled in the art at the time the instant application was filed.¹ However, Applicants submit that the Action has mischaracterized the evidence of record.

The Action states that “applicant in his response argues that while both articles (referring to De La Paz and Delcourt) acknowledge the oxidative mechanism may play a role in the development of AMD, neither of these references teach that superoxide can be used to treat macular degeneration” (instant Office Action, page 2). However, the Action appears to mischaracterize Applicants’ remarks relative to the teachings of these references, as well as the teachings themselves. In particular, the Action states that “the fact that the references (referring to De La Paz and Delcourt) recognize that superoxide dismutase is involved in protecting against oxidative damage such as that which leads to AMD, is sufficient for a person skilled in the art to use such compounds for the treatment of AMD.” However, there are numerous oxidative mechanisms involving a large universe of oxidative compounds, including numerous oxidative enzymes and antioxidants. De La Paz and Delcourt do not narrow the universe to superoxide dismutases. On the contrary, these references teach away from such a narrowing by concluding that there is no significant association between disease severity of AMD and superoxide dismutase activity, and that high levels of erythrocyte superoxide dismutase activity were not associated with late AMD and early signs of AMD (see discussion on pages 3 and 4 of Applicants’ Response submitted June 25, 2008).

MPEP §2143.02 (II) states that “the test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts. Where the teaching of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another.” In view of the totality of the art at the time the instant application was filed, there was no reason for one of skill in the art to expect that superoxide dismutase compounds could be used to treat AMD, even in view of Winkler *et al.*

The Federal Circuit in *Eisai Co. v. Dr. Reddy’s Labs* indicated that “the Supreme Court’s analysis in *KSR* presumes that the record before the time of invention would supply some

¹ Applicants presented evidence in the form of the teachings of De La Paz and Delcourt, which were discussed in Applicants’ Responses submitted August 1, 2007, October 1, 2007, and June 25, 2008

reasons for narrowing the prior art universe to a ‘finite number of identified, predictable solutions.’” (*Eisai Co. v. Dr. Reddy’s Labs, Ltd.*, 487 USPQ2d 1452 (Fed. Cir. 2008) citing *KSR Int’l Co. v. Teleflex*, 127 S. Ct. at 1742. The Supreme Court in *KSR Int’l v. Teleflex Inc.* stated that “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR Int’l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). As mentioned above, the universe of compounds that may be involved in oxidative mechanisms is very large. The Action has not pointed out any reasons based on the aforementioned relied upon references or anything else that would have motivated one of skill in the art to select the compounds of the instant invention out of the vast universe of oxidant scavengers and antioxidants to treat macular degeneration, diabetic retinopathy, or retinal edema. Thus, the Action fails to provide an articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. The teachings of the relied upon references are not sufficient to support the Action’s conclusion that it would have been obvious to use any superoxide dismutase compounds to treat macular degeneration, diabetic retinopathy, or retinal edema.

In light of the foregoing arguments, Applicants submit that the Action has erred in combining the cited references to arrive at the instant invention. Consequently, Applicants respectfully request that the obviousness rejection be withdrawn.

C. Conclusion

This is submitted to be a complete response to the outstanding Action. The Examiner is invited to contact the undersigned attorney at (817) 615-5330 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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